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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/940,878	08/29/2001	Emmanuel Lazaridis	1372.61.PRCWOUS	5633

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EXAMINER
MILLER, MARINA I

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 05/26/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

	Application No.	Applicant(s)
Office Action Summary	09/940,878	LAZARIDIS, EMMANUEL
	Examiner	Art Unit	
	Marina Miller	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE <u>3</u> MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on <u>01 April 2005</u>.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) <u>1-36</u> is/are pending in the application.

    4a) Of the above claim(s) <u>1-20 and 24-36</u> is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) <u>21-23</u> is/are rejected.

7) ☐ Claim(s) <u>21-23</u> is/are objected to.

8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☒ The drawing(s) filed on <u>29 August 2001</u> is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.

    Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

    Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

    a) ☐ All b) ☐ Some * c) ☐ None of:

      1. ☐ Certified copies of the priority documents have been received.

      2. ☐ Certified copies of the priority documents have been received in Application No. _____.

      3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

    * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)

2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date <u>6/26/2002</u>.

4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .

5) ☐ Notice of Informal Patent Application (PTO-152)

6) ☐ Other: _____.

S-O-O

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group IV (claims 21-23) and a disease species of

Species B in the replies filed on 5/1/2005 is acknowledged.

Claims 1-20 and 24-36 are withdrawn from further consideration pursuant to 37 CFR

1.142(b), as being drawn to a nonelected species and Groups, there being no allowable generic or

linking claim.

An action on the merits of claims 21-23, as they read on the elected species, follows.

Information Disclosure Statement

Information Disclosure Statement (IDS) filed 6/28/2002 has been considered.

Drawings

The drawings are objected to because figures 1, 4, and 6 are poor quality. Figures 1 and 6

are too light and figure 4 is too dark so that one cannot appreciate information presented on these

figures. Also, labels on figures 1, 4(a)-(b), and 6 are in very small print that it is not suitable for

reading. The specification indicates that figure 1 and 4 are color photographs. It is noted that no

color photographs have been submitted.

If applicant has not previously submitted color photographs and desires to submit,

applicant is advised that color photographs and color drawings are not accepted unless a petition

filed under 37 CFR 1.84(a)(2) is granted. Any such petition must be accompanied by the

appropriate fee set forth in 37 CFR 1.17(h), three sets of color drawings or color photographs, as

appropriate, and, unless already present, an amendment to include the following language as the

first paragraph of the brief description of the drawings section of the specification:

> The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the Office upon request and payment of the necessary fee.

Color photographs will be accepted if the conditions for accepting color drawings and

black and white photographs have been satisfied. See 37 CFR 1.84(b)(2).

Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to

the Office action to avoid abandonment of the application. Any amended replacement drawing

sheet should include all of the figures appearing on the immediate prior version of the sheet,

even if only one figure is being amended. The figure or figure number of an amended drawing

should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure

must be removed from the replacement sheet, and where necessary, the remaining figures must

be renumbered and appropriate changes made to the brief description of the several views of the

drawings for consistency. Additional replacement sheets may be necessary to show the

renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an

application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet"

pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will

be notified and informed of any required corrective action in the next Office action. The

objection to the drawings will not be held in abeyance.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 21-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 21 recites a "formula" that contains a symbol "~" which usually means "proportional" or "approximately equal." It is not clear what this symbol means in the formula. Further, "formula" might mean an "equation" and would require sign "=" between the left and the right part of the equation. Applicant refers on p. 42 of the specification to the same mathematical expression as to "model with <u>forms</u> like...." Also, the formulas of claim 21 comprises a symbol "+" in the expression $N[t_{il} + f(\alpha,\beta,\gamma)...]$. However, the specification discloses the same formula wherein the expression is $N[f(t_{il}, \alpha,\beta,\gamma)...]$ on p. 26 and $N[t_{ij} f(\alpha,\beta,\gamma)...]$ on p. 42. It is not clear what expression is actually intended in claim 21. The formula of claim 21 comprises "σ" which is not defined in the specification. For the reasons stated above, claim 21 is indefinite.

Claim 22 comprise an expression $N[.]$. The term "$N[.]$" is not recited in parent claim 21, therefore there is no antecedent basis for the term, and claims 22 is indefinite. Further, the term "$N[.]$" is not defined by the specification or claims. Parent claim 21 recites $N[t_{il} + f(\alpha_{mi},\beta_{lj},\gamma_{ml}, \sigma^2]$ as part of a formula or equation. If $N[.]$ is intended to limit the formula of claim 21, then it is further unclear what limitation is intended by limiting a particular term or variable to "refer" to a Gaussian distribution. For the reasons stated above, claim 22 is indefinite. Claim 23 depends from claim 21 and, therefore is also indefinite.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all

obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 21-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Alon,

PNAS, 96:6745-6750 (1999), in view of Lazaridis, E., Discrimination and classification using

conditionally independent marginal mixtures, *A Dissertation Thesis*, Chicago, The University of

Chicago, Illinois, December 1994, and further in view of Skene, *Statistics in Medicine*, 11:2111-

2122 (1992).

Alon discloses a method for gene expression pattern analysis to help identify families of

genes and tissues based on expression pattern in the data set (p. 6749, right col.). Alon analyzed

40 colon tumor and 22 normal samples and obtained expression profiles for more than 6,500

human genes (p. 6745). Alon' method comprises steps of recording a matrix of gene expression

(p. 6746, right col, and fig. 2-3), providing measurements on tissues samples (p. 6745, and fig. 2-

3), classifying genes into functional groups and classifying tissues based on their gene expression

similarity (p. 6745, right col.), and calculating probability that each gene is a member of a cluster

for the first direction and a cell or tissue is a member for each cluster of the second direction (p.

6746, right col.; for cell-line cluster, *see* p. 6749, left col.). Alon analyses gene expression of

tumor and normal tissues (a cellular phenotype, *e.g.*, a disease) (p. 6745).

Alon does not teach a model described by the formula recited in instant claim 21.

Lazaridis teaches a model used for statistical analysis of a sample comprising N objects, each of which has J measured characteristics (p. 1). His model associates objects (people) with attributes (diseases) (Abstract). The data for each object consist of measurements (*e.g.*, laboratory tests). Lazaridis modeled a cluster in the data by latent class (p. 4). Lazaridis applied his model to a group of patients suffering from a variety of diseases. Lazaridis' model allows associating a patient with a disease and characterizing the disease by comparing data from a patient with a standard (p. 6-7). Lazaridis discloses a latent class formula similar to that of the instant invention (p. 7, expression 1.2.1, p. 9, expression 1.2.3) wherein μ and σ are the latent class parameters similar to $(t_{ij,}\ \alpha,\beta,\gamma,\ \sigma)$ of the instant invention (p. 9, 37, and 38). Lazaridis discloses calculating a likelihood that an object belongs to a subset of a particular characteristic (for example, p. 37 and p. 78). Lazaridis illustrates his model on the thyroid data consisting of the results of five laboratory tests specific for thyroid disease obtained from 215 patients (p. 114).

Although Lazaridis discloses the latent class parameters μ and σ, he does not specifically disclose parameter estimation for two directions.

Skene teaches a latent class model for repeated experimental measurements wherein a specific response is measured at a particular time (a two directional experiment) (p. 2113). Skene discloses parameters of the response $(\mu_{jm},\ \delta_{il},\ p_{ij},\ \sigma^2)$ (p. 2114).

It would have been obvious to one skilled in the art at the time of the invention to modify the method of Alon to apply a latent class model for analysis biological data, such as taught by Lazaridis and Skene, where the motivation would have been to improve correlation of data

obtained from an object and an attribute, as taught by Lazaridis (Abstract, p. xi) and Skene, p. 2120.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marina Miller whose telephone number is (571)272-6101. The examiner can normally be reached on 8-5, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, Ph. D. can be reached on (571)272-0718. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Marina Miller
Examiner
Art Unit 1631

MARJORIE A. MORAN
PRIMARY EXAMINER

MM

5/19/05